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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Ni et al.

Application Serial No.: 09/911,346 Art Unit: 1646

Filed: July 24, 2001 Examiner: Mertz, P.

For: Antibodies to Natural Killer Cell Enhancing Factor C Attorney Docket No.: PF199D2

Declaration of Viktor Roschke Under 37 C.F.R. § 1.132

Sir:

I, Viktor Roschke, Ph.D., hereby declare and state as follows:

1. I am currently employed as the Director of Clinical Immunology and Antibody Development at Human Genome Sciences, Inc. (HGS), which I understand to be the assignee of the above-captioned patent application (the '078 Application). I received my MS degree in Biochemistry in 1977 from the Novosibirsk University. I earned my Ph.D. in 1985 from the Novosibirsk Institute of Bioorganic Chemistry of the Russian Academy of Sciences after completion of 5 years of research in the field of immunochemical analysis of biomolecules. This research entailed extensive antibody development work. From 1985 to 1992, I conducted independent research in monoclonal antibody development and applications of immunochemical techniques to understanding the structure and function of biomolecules. I also was involved significantly in implementation of new immunochemical techniques for use in medical diagnostics. In 1992, I joined the Laboratory of Genetics at National Cancer Institute (NCI) in Bethesda, Maryland. I spent 5 years at NCI studying the biology of antibody-producing B cell tumors known as plasmacytomas. In 1997, I joined Human Genome Sciences where my research work included, in large part, both carrying out and supervising the development and characterization of therapeutic and reagent antibodies in support of pre-clinical and clinical research on protein and antibody-based therapeutics. I

have co-authored a book chapter and 36 scientific articles that have been published in peer-reviewed scientific journals. A copy of my curriculum vitae is attached as **Exhibit A**.

2. I have been shown and have examined U.S. Patent Application No. 09/911,346 (the '346 Application), captioned above, which I understand was filed on July 24, 2001 and has an effective filing date of June 6, 1995. I will refer to the '346 Application as "the Application."

3. I have been shown and have examined U.S. Patent No. 5,250,295 (the '295 Patent) entitled Natural Killer Cell Enhancing Factor by Shau et al. I will refer to this patent as the "'295 Patent." A copy of the '295 Patent is attached hereto as **Exhibit B**.

4. I have been shown and have examined U.S. Patent No. 5,610,286 (the '286 Patent) entitled DNA's Encoding Natural Killer Cell Enhancing Factor by Shau et al. I will refer to this patent as the "'286 Patent." A copy of the '286 Patent is attached hereto as **Exhibit C**.

5. I have been asked by patent counsel for HGS to provide my expert opinion as to whether the antibodies disclosed in the '295 and '286 Patents by Shau et al. would have been characterized by those who ordinarily practiced research with antibodies at the effective filing date of June 6, 1995, as an antibody that specifically binds the protein NKEF C of SEQ ID NO:2 or the protein encoded by the cDNA contained in ATCC Deposit No. 97157 or a fragment thereof.

"Specifically Binds" As Understood by Those Using Antibodies in Research

6. Those who ordinarily practice research with antibodies (for example, those who practice research in areas such as immunology and cell & molecular biology), both now and at the time of the effective filing date, routinely use the phrase "specifically binds" to refer to the functional ability of the antibody to preferentially bind a particular (target) antigen instead of a non-target antigen. As an example, the textbook *Immunology: a Synthesis* by Edward Golub and Douglas Green (2nd edition, Sunderland, MA:Sinauer Associates, Inc.1991:p. 23, attached herewith as **Exhibit D**) defines specificity as "the ability of antibodies produced in response to an antigen to react with that antigen and not with others."

7. Thus, an antibody that specifically binds a given protein (herein after Protein X, the target antigen) is an antibody that preferentially binds Protein X without a significant level of binding to other proteins (*i.e.*, without a significant level of "cross-reactivity" or "cross-reaction"). In this context "preferentially binds" "without a significant level of binding" to other antigens means that the antibody's ability to specifically bind the target antigen makes it useful for discriminating the target antigen from other antigens in biological assays, diagnostic assays, or treatment protocols (such as in cell staining, immunoblot analyses, immunoprecipitations, enzyme-linked immunosorbent assays (ELISA), or *in vivo* binding of the target antigen).

8. An antibody that binds equally well to Protein X and paralogous[1] polypeptide Protein Z would not be an antibody that an immunologist would consider as one that specifically binds Protein X, regardless of the sequence identity between the two proteins. Consider, for example, the *Santa Cruz Biotechnology Research Antibodies 1997/98 Catalog*, which lists many antibodies that are specific for a protein and are non cross-reactive to other members of the protein family. For example, the catalog lists an Anti-FGF-1 (fibroblast growth factor 1) antibody and describes it as "specific for FGF-1; non cross-reactive with other members of the FGF family." As another example, the catalog lists an Anti-CKR-1 (C-C chemokine receptor 1) antibody and describes it as "specific for CKR-1; non cross-reactive with other known C-C chemokine receptor gene-encoded proteins." *See, Santa Cruz Biotechnology, Inc. 1997/98 Research Antibodies Catalog*, pages 239 and 319, respectively, enclosed herewith as part of **Exhibit F**. The usage of the term "specifically binds" as I have described it is consistent with the usage of the term as of June 6, 1995.

9. Members of either the FGF family or C-C chemokine receptor family share a high degree of homology with each other. Yet antibodies specific for individual members of

[1] The terms "orthologous" and "ortholog/orthologue" versus "paralogous" and "paralog/paralogue" are used herein as these terms are generally understood and in accord with a definition provided by the National Center for Biotechnology (NCBI). *See* the NCBI Field Glossary available on the internet at http://www.ncbi.nlm.nih.gov/Class/FieldGuide/glossary.html#A, a printout of the excerpted definitions for orthologue and paralogue are attached herewith as **Exhibit E**. Orthologous genes (or, genes which are orthologues) are derived from a common ancestor through vertical evolutionary descent. Thus, genes (and proteins encoded by them) are considered to be orthologues when they represent the *same* gene (or protein) found in *different* species. For example, feline FGF-1 (fibroblast growth factor-1), murine FGF-1, and human FGF-1 are orthologues (orthologous proteins). In contrast, paralogous genes (or, genes which are paralogues) are genes found within the same genome that are thought to have evolved by gene duplication. For example, human FGF-1, human FGF-2, and human FGF-3 are gene paralogues; and, the proteins encoded by these genes are also paralogues (or paralogous proteins).

this family are expressly advertised as not cross-reacting with other members of the family (paralogues). This illustrates my point, that scientists who routinely work with antibodies consider an antibody that is "specific" for one member of a protein family as one that does not appreciably bind, i.e. cross-react, with other members of that family (i.e., paralogues) irrespective of the level of sequence identity among family members.

10. In contrast, the fact that an antibody specifically binds a polypeptide in one species (*e.g.*, human) also binds the orthologous polypeptide in another species (*e.g.*, mouse) would not change an immunologists' characterization of that antibody as "specific". Thus, an antibody that specifically binds human Protein X may also specifically bind murine Protein X. Such cross-species binding merely indicates that the antigenic determinant to which the Protein X antibody binds is conserved in both human and mouse Protein X. Likewise an antibody that is specific for Protein X may bind fragments or variants of Protein X depending on the presence or absence of the antigenic determinant of the protein of SEQ ID NO:2 or encoded by the cDNA contained in ATCC Deposit No. 97157 included in the fragment or variant.

11. To summarize, scientists routinely working with antibodies, as of June 6, 1995, would define an antibody that specifically binds a protein as an antibody that under empirically optimized antibody binding conditions:

a) is useful in biological assays, diagnostic assays, or therapeutic protocols because of its ability to discriminate between the target protein and non-target proteins; and

b) binds the protein (as well as fragments and variants of the protein which contain the antigenic determinant) against which it was raised/screened with significantly higher affinity than it binds other proteins (*i.e.*, paralogues and unrelated proteins).

Antibodies Described in the '286 Patent are Not Antibodies That Specifically Bind NKEF C

12. The present Application describes a Natural Killer Cell Enhancing Factor C protein having the amino acid sequence of SEQ ID NO:2 or of the protein encoded by the cDNA contained in ATCC Deposit No. 97157 that is known in the literature as NKEF C. For the purposes of this declaration, I will henceforth use the term "NKEF C" to refer to either or

both the protein of SEQ ID NO:2 or the protein encoded by the cDNA contained in ATCC Deposit No. 97157. NKEF C is member of a family of Natural Killer Cell Enhancing Factors (NKEFs), of which proteins known as NKEF A and NKEF B are also members. An alignment of these proteins is shown in **Exhibit G**.

13. The '295 and '286 Patents collectively describe purified and characterized NKEF A and B. More particularly, inventors purified a factor from human peripheral blood lymphocytes (PBL), which they termed "NKEF." The purity and molecular weight of their purified NKEF protein was determined by SDS-PAGE (see '286 Patent, column 9, paragraph 3). The band corresponding to NKEF on the SDS-PAGE gel was excised and used as an immunogen to immunize rabbits for the generation of a rabbit anti-NKEF polyclonal serum. This polyclonal antibody was used to clone a cDNA encoding an NKEF polypeptide from a cDNA expression library (see '286 Patent, column 13, paragraph 1). The cDNAs isolated from this immunological screening/cloning procedure that allowed the inventors to obtain the first NKEF protein were used to obtain further NKEF cDNAs. The ultimate results of the '286 Patent identified two proteins: NKEF A and B shown in SEQ ID NOS. 2 and 4, respectively. From the specification of the '286 Patent it is not clear whether the rabbit antibody was raised against NKEF A or B or if the antibody is able to bind both A and B. It is certain their antibody binds at least one of NKEF A and B.

14. Nether the '295 nor the '286 Patent identifies the NKEF C of the present application, nor do they test whether the antibodies described in the '295 and '286 Patents bind NKEF C. The antibodies disclosed in the Shau Patents may or may not bind NKEF C. Such a determination cannot be predicted and can only be determined experimentally. However, the ability of these antibodies to bind NKEF C is immaterial to the question of whether these antibodies are antibodies that specifically bind NKEF C. As discussed above, an antibody that specifically binds a protein does not significantly or appreciably bind a paralogue of that protein. In the present context, an antibody that specifically binds NKEF C would not significantly or appreciably bind the paralogues of NKEF C, namely NKEF A and B. Because the antibodies described in Shau et al. bind NKEF A and B, they are clearly not antibodies that specifically bind NKEF C. Those who ordinarily practice research with antibodies would have come to this conclusion at the effective filing date of June 6, 1995.

15. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patents issuing thereupon.

19 Mar 04

DATE

VIKTOR ROSCHKE, PH.D.

CURRICULUM VITAE

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Education

1985, Ph.D. (Molecular Biology). Institute of Bioorganic Chemistry. Novosibirsk, Russia.
Thesis: Development of new methods of immunoanalysis using human myoglobin as a model protein.
1977, M.S. (Biochemistry). Novosibirsk University, Novosibirsk, Russia.

Research experience

1997-Present. Human Genome Sciences, Inc. Rockville, MD.

1997-1998 - Scientist, Cell biology,
1998-2001 - Section Head, Antibody Development
2001-2003 - Associate Director, Antibody Development
2003-Present – Director, Clinical Immunology and Antibody Development.

Currently supervise a group of 42 employees.
Responsible for antibody and ELISA development to support pre-clinical and clinical studies on novel therapeutic proteins and antibodies. Developed antibodies and ELISA assays for more than 30 proteins in early pre-clinical development. Supervise development and qualification of late stage pre-clinical and clinical PK, immunogenicity and neutralization assays for PAmAb, ETR-2, TR2-J, ETR-1, anti-CCR5 mAb, Albuferon.
Since 1999 started a program of generation and characterization of human therapeutic antibodies using Xenomouse technology. The main interest is concentrated on antibodies to TNF-family members and integral transmembrane proteins (7 TMs).
Identified and characterized several new cancer specific targets for antibody mediated immunotherapy using electronic library class analysis of the HGS database.

1992-1997. Lab. of Genetics, NCI, NIH. Bethesda, MD. Visiting Associate.

Conduct research on cellular and molecular mechanisms of development and dissemination of murine B-cell tumors. Main fields of activity are:
Studies on structural aspects of interaction of primary plasma cell tumors with stromal elements of the inflammatory granulomatous tissue (establishing primary cultures of stromal cells from mouse granuloma tissu)..
Generation of rat and rat x mouse monoclonal antibodies, screening MAB by ELISA on immobilized primary stromal cells and by immunohistochemical staining of cloned stromal cells, selection of specific clones by immunoperoxidase staining of frozen sections of different tissues.

Investigation of c-myc genomic instability by frequency determination of spontaneous and cholera toxin induced chromosomal translocations in mice susceptible and resistant to plasmacytomagenesis (single copy Long distance PCR followed by Southern blot analysis using "nested" oligonucleotide probes). Assessment of the role of Il-4 and γ-interferon in plasmacytoma development by tumor induction experiments in Il-4 and γ-interferon knockout mice (viral tumor induction, ***tumor phenotyping by FACS analysis, ELISA, RFLP analysis and histochemistry).***

Investigation of disseminated growth of murine plasmacytoma with particular attention to the question of bone marrow involvement (construction of tagged cell lines, intravenous injection in mice, dissection of mice, preparing tissue specimens for paraffin sections and DNA isolation, ***detection of metastases by PCR and immunohistochemistry,*** *assessing the bone marrow involvement and bone resorption by microscopic analysis of specially stained paraffin sections).*

Generation of "knockout" mice using homologous recombination technology (preparation and characterization of targeting constructs, transfection and selection of embryonic stem cells, limited experience in blastocyst injection and reimplantation into foster mothers). Investigation of the role of different genes (CD44, Sα and Pvt-1) in plasmacytomagenesis.

1988-1992. Director, Research and Development. BioSAN Inc., Institute of Bioorganic Chemistry, Siberian Branch of the USSR Academy of Sciences, Novosibirsk.

Responsible for Research and Development of a small company affiliated with an academic institution. Supervise a group of 15 employees including 5 doctoral level biologists and chemists. Major directions include ***development of new immunochemical methods for research and diagnostic purposes,*** *development of an universal approach for random tritium labeling of organic compounds and biopolymers, development of an ultrafast oligonucleotide synthesizer.*

Personal research interests concentrate on development of monoclonal antibodies and new immunochemical methods for detection of low molecular weight toxicants.

1987-1989. Lab chief. Laboratory of Immunochemistry and Cellular Engineering, Institute of Bioorganic Chemistry and affiliate Institute of Clinical Immunology, Siberian Branch of the USSR Academy of Sciences, Novosibirsk.

Provided scientific and administrative leadership for 7 employees including 2 postdoctoral biochemists. The main purposes of the laboratory were facilitation of collaboration between academic and clinical institutions, developing new diagnostic tools, and establishing a training program for medical school graduates.

Conducted research on time resolved fluoroimmunometric analysis. Involved in immunochemical studies of the topography and functional mapping of RNA-polymerases from different species, using monoclonal antibodies.

1984-1987. Staff Scientist. Institute of Bioorganic Chemistry, Siberian Branch of the USSR Academy of Sciences. Novosibirsk.

Established hybridoma technology using domestic reagents and components (one of the first groups in USSR to establish hybridoma technology). Generated monoclonal antibodies against a variety of antigens including human myoglobin, tick borne encephalitis virus, E.coli and Wheat germ RNA-polymerases. Developed an original method for localization of antigenic determinants in proteins with known primary structure by means of limited protein hydrolysis and immunochemical staining of Western blots.

1979-1984. Institute of Organic Chemistry, Siberian Branch of USSR Academy of Sciences. Novosibirsk. Research Fellow, since 1981 - Junior Scientist.

Conduct research on new principles of immunoanalitical techniques. Developed a rapid method of nonequilibrium radioimmunoassay of human myoglobin for express diagnostics of myocardial infarction.

Synthesized ATP conjugates with thyroxine and myoglobin and developed a new technique of ATP-metric bioluminescent immunoassay. Proved the possibility to use complement mediated antigen-antibody specific lysis of liposomes as an immunoanalytical tool.

Developed technologies for industrial production of RIA kits for myoglobin and insulin.

1975-1979. Institute of Cytology and Genetics, Siberian Branch of USSR Academy of Sciences, Novosibirsk. Research Student, since 1977 - Research Fellow.

Research on molecular mechanisms of steroid hormones action. Demonstrated increasing of in vitro translation activity of mRNA preparations from rat liver upon hydrocortisone administration

Specific areas of expertise:

Antibody development.

Involved in Antibody development since 1979.

During the last six years supervised the generation and characterization of MABs against more than 30 proprietary HGS proteins.

Generated and characterized MABs against a number of haptens, protein, viral and cellular antigens: 2,3,7,8 - tetrachlorodibenzodioxine, myoglobin, murine G-6-PDH (allele specific), RNA polymerase from E.coli (different subunits), RNA-polymerase from wheat germs (different subunits, topographic determinants), tick born encephalitis virus (different proteins, topographic determinants), murine stromal cells (surface specific, lineage specific, tissue specific).

Generated and characterized human monoclonal antibodies against a more than 10 proprietary HGS targets using Xenomouse technology. Experience in generation of Mabs against integral transmembrane proteins.

Established an efficient strategy of generation of poly and monoclonal anti-idiotypic antibodies in rabbits and mice.

Assay development.

Supervised Development and Qualification of PK, immunogenicity and neutralization assays in a GLP compliant environment.

Established a number of assays for screening and characterization of murine and human (both phage display and Xenomouse) antibodies – affinity ranking, receptor binding, real time kinetics (BIACore), cell surface binding, complement fixation, complement and cell mediated antibody cytotoxicity, cell proliferation, cell viability.

Established a strategy for screening MAB against cell surface antigens of stromal cells (ELISA and DELFIA on immobilized cells of different lineages; high-throughput FACS analysis, immunostaining on tissue culture clusters, frozen and paraffin sections; Western blot analysis of cell extracts).

Established assays for pre-clinical and clinical PK, immunogenicity and neutralization studies for more than 20 different proteins and antibodies.

Developed a method for mapping MAB epitopes on proteins (limited enzymatic or chemical degradation of the protein of interest, separation of peptides by PAGE and subsequent Western blot immunostaining). Characterized epitopes for MAB against human myoglobin, RNA polymerases from E.coli, wheat germs, and V3 protein from tick-borne encephalitis virus).

Scientific publications.

Book chapter:

Grachev M.A., Roschke V.V. ATP-metric immunoanalysis. *In:Luminescence immunoassay and molecular applications*, p203-215, K.Van Dyke, R.Van Dyke Eds. CRC Press, Boca Raton, 1990.

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Roschke V.V., Laktionov P.P, Nechaeva M.V., Rykova E.Yu. A hybrid cell line derived from *Mus Musculus L.* producing monoclonal antibodies to human myoglobin.

IMMUNOLOGY
A SYNTHESIS
Second Edition

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Scripps Clinic and Research Foundation

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PART-OPENING ELECTRON MICROGRAPHS

Part 1 (page 19): Antibody–hapten complex (purified rabbit anti-2,4-dinitrophenyl antibody and a bivalent hapten). [From Valentine and Green, 1967. *J. Mol. Biol.* 27: 615]

Part 2 (page 191): A resting lymphocyte, probably a T cell (×21,800). [Courtesy of D. Zucker-Franklin, New York University Medical Center]

Part 3 (page 543): Immune complexes, seen as electron-dense, hump-shaped deposits in the upper third of the photo, along a capillary wall in a glomerulus following streptococcal glomerulonephritis (×17,250). [Courtesy of M. N. Yum, Indiana University Medical Center]

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free hapten. In general, carriers are molecules that are of themselves immunogenic. Hence we may think of the hapten as an added determinant on an already immunogenic molecule. The study of hapten–carrier systems has given us much information about the nature of antigens and the antigen–antibody interaction, but it has also been one of the keys to understanding the cellular events in the immune response (see Chapter 17).

The Specificity of Serological Reactions

Landsteiner studied haptens and carriers in an attempt to work out the rules that govern antigenicity. The compilation of these studies appeared in his classic treatise, *The Specificity of Serological Reactions*. As we will see, no universal rules governing antigenicity came out of this work, but what did emerge was the realization that the chemical properties of the antigen molecule determine the specificity of the immune system. SPECIFICITY is defined as the ability of antibodies produced in response to an antigen to react with that antigen and not with others. The thoroughness of Landsteiner's approach and the elegance of his thought make browsing in this volume, which is available in paperback, a worthwhile experience for any scientist.

Landsteiner immunized a rabbit with a hapten–carrier conjugate. This injection resulted in antiserum with both anti-hapten and anti-carrier activity. He then conjugated the hapten to a different carrier and reacted the conjugate with the same antiserum to test for the presence of *anti-hapten* antibodies. Because he had changed carrier molecules for the test, there was no anti-carrier reaction; the reaction observed was between the anti-hapten antibodies and the hapten. He then varied the properties of the hapten in order to study, for example, the effect of acidic or ionic groups on the ability of the antibody raised against the original hapten to react with the modified hapten. Although no general rules emerged, it is instructive to look at some of Landsteiner's conclusions (Landsteiner, 1962):

> The principal results of numerous precipitin tests with azoproteins were the following . . .
>
> 1. First of all, the nature of the acidic groups was of decisive influence. [p. 163]

Data from Landsteiner's experiments are shown in Tables 1–4. Antibody is raised against aminobenzene or aminobenzene with

Cross Reactivity

Antibody molecules can exhibit great specificity, but there are CROSS REACTIONS—cases in which antibody to antigen A also reacts with antigen B. This can be due to the presence of the same molecular configuration, or ANTIGENIC DETERMINANT, on the two antigens, or to properties of a determinant that allow it to be recognized as though it were another group. Antigenic determinants are also called *epitopes*. As we move through the book we will use these terms almost interchangeably. We can conceive of molecules that have similar but not identical structures and appear in closely related species. These molecules may have enough similarity to allow antibodies against one to react with the other.[1]

Table 5 shows the percentage of cross reactivity between albumins of different species. Antibody was made against bovine serum albumin (BSA), and the extent of the ability of albumins from other species to react with the anti-BSA was then determined. This cross reactivity is probably due to the presence of common determinants on the different albumins. To determine this, however, each of the determinants must be isolated and studied chemically. Even then, as we will see later in this chapter, we cannot be quite certain of

[1] The neurobiologist A. K. Hall has suggested the term IMMUNOFREQUENT for such determinants.

Table 5 Cross reaction between BSA and other albumins.[a]

Albumin source	Percentage of cross reactivity with BSA	Albumin source	Percentage of cross reactivity with BSA
Human	15	Mouse	10
Pig	32	Rat	13
Sheep	[illegible]	Hamster	13
Horse	13	Cat	25
Guinea pig	[illegible]	Vallaroo	[illegible]
Dog	13		

Source: Data from Weigle, 1961. *J. Immunol.* 87: 599.

[a] Rabbit anti-BSA was absorbed with each of the albumins listed and then tested for its ability to react with BSA. This ability is expressed as a percentage *cross reactivity*. The data show that sheep BSA has the highest amount of cross reactivity and guinea pig and vallaroo the least.

O

Top

Orthologue

Orthologues are genes derived from a common ancestor through vertical descent. This is often stated as the same gene in different species. In contrast, paralogs are genes within the same genome that have evolved by duplication.

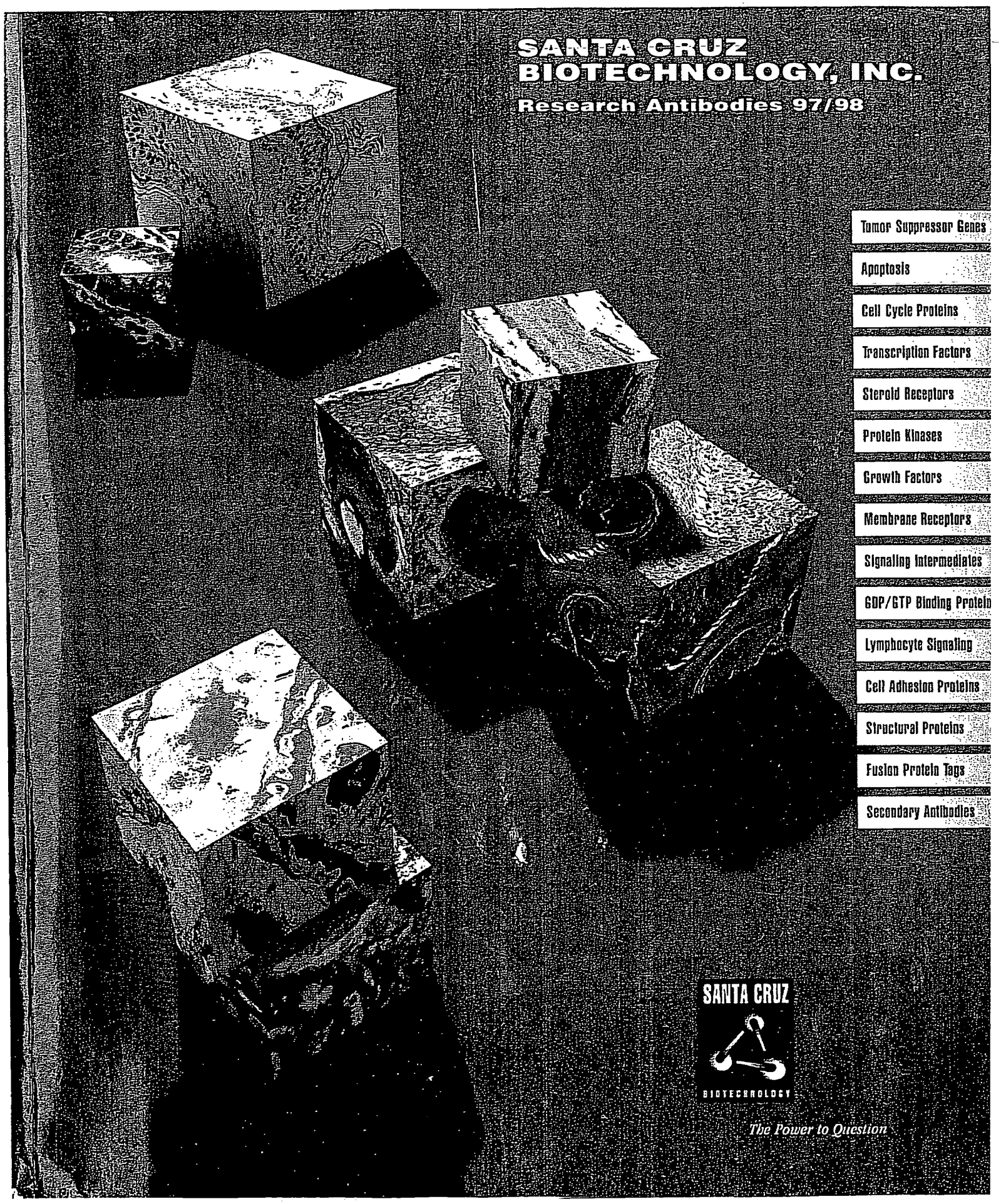
The hemoglobin genes are a good example. Two separate genes (proteins) make up the molecule hemoglobin (alpha and beta). The alpha and beta DNA sequences are very similar and it is believed that they arose from duplication of a single gene, followed by separate evolution in each of the sequences. Alpha and beta are considered paralogs. Alpha hemoglobins in different species are considered orthologs.

P

Top

Paralog

Paralogs are usually described as genes within the same genome that have evolved by duplication. See Ortholog.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Lymphocyte Signaling
Cell Adhesion Proteins
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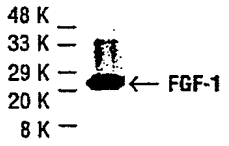
The Power to Question

Fibroblast Growth Factors

Fibroblast growth factors (FGFs) share 30-55% sequence identity and similar gene structure and are capable of inducing transformation via an autocrine mechanism when introduced into cells expressing the appropriate FGF receptor. Acidic (aFGF/FGF-1) and basic FGF (bFGF/FGF-2), prototypes of this expanding family of growth regulatory molecules, are well known for their ability to stimulate the proliferation of cells of mesenchymal, epithelial and neuroectodermal origin. FGF-3 (Int2) and FGF-4 (Hst/Kaposi FGF) are encoded by proto-oncogenes. Thus, FGF-4 was first revealed to be an oncoprotein in Kaposi's sarcoma cells, while the Int2 gene encoding FGF-3 is oncogenically activated by insertional mutagenesis during mouse mammary tumor virus-induced carcinogenesis. Other family members include FGF-5, FGF-6, FGF-7 (keratinocyte growth factor, KGF), FGF-8 (AIGF) and FGF-9 (GAF).

FGF-1 (C-19): *cat # sc-1884*

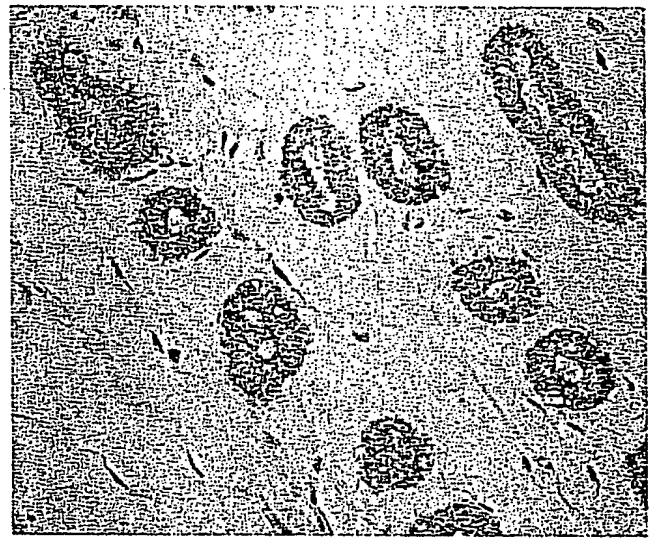
- goat polyclonal IgG, 200 µg/ml: $175
- epitope corresponding to amino acids 137-155 mapping at the carboxy terminus of the fibroblast growth factor-1 (FGF-1) precursor of human origin (identical to corresponding mouse and rat sequences)
- specific for FGF-1; non cross-reactive with other members of the FGF family
- mouse, rat and human reactive
- Western blotting and ELISA
- blocking peptide available (sc-1884 P), 100 µg/0.5 ml: $45



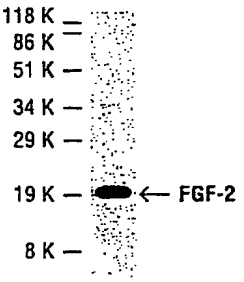
FGF-1 (C-19): sc-1884. Western blot analysis of human FGF-1: sc-4130 WB.

FGF-2 (147)-G: *cat # sc-79-G*

- goat polyclonal IgG, 200 µg/ml; also available as rabbit IgG, 100 µg/ml, FGF-2 (147): sc-79: $175
- epitope corresponding to amino acids 40-63 mapping within the amino terminal domain of the FGF-2 precursor of human origin (differs from corresponding mouse and chicken sequences by a single amino acid)
- basic FGF specific; non cross-reactive with acidic FGF
- mouse, rat and human reactive
- Western blotting, immunoprecipitation and immunohistochemistry (formalin-fixed, paraffin-embedded tissues)
- blocking peptide available (sc-79 P), 100 µg/0.5 ml: $45



FGF-2 (147): sc-79. Immunoperoxidase staining of formalin-fixed, paraffin-embedded porcine uterine tissue. Kindly provided by Laurie A. Jaeger.



FGF-2 (147): sc-79. Western blot analysis of human FGF-2: sc-4131 WB tested at 10 ng.

C-C Chemokine Receptors

The C-C or β chemokine family is characterized by a pair of adjacent cysteine residues A total of seven C-C chemokine receptors have been identified. CKR-1, CKR-2A, CKR-2B, CKR-3, CKR-4, CKR-5 and the Duffy blood group antigen Each of these receptors are G protein-coupled, seven pass transmembrane domain proteins whose major physiological role is to function in the chemotaxis of T cells and phagocytic cells to sites of inflammation. These receptors also serve as coreceptors for viruses.

CKR-1 (C-20): *cat # sc-6125*

- goat polyclonal IgG, 200 µg/ml: $175
- epitope corresponding to amino acids 336-355 mapping at the carboxy terminus of the C-C chemokine receptor gene type 1 (CKR-1) precursor of human origin (differs from corresponding mouse sequence by two amino acids)
- specific for CKR-1; non cross-reactive with other known C-C chemokine receptor gene-encoded proteins
- mouse, rat and human reactive
- Western blotting and immunohistochemistry
- blocking peptide available (sc-6125 P), 100 µg/0.5 ml: $45

CKR-2A (C-17): *cat # sc-6227*

- goat polyclonal IgG, 200 µg/ml: $175
- epitope corresponding to amino acids 358-374 mapping at the carboxy terminus of the C-C chemokine receptor gene type 2A (CKR-2A) precursor of human origin
- specific for CKR-2A; non cross-reactive with other known C-C chemokine receptor gene-encoded proteins
- human reactive
- Western blotting and immunohistochemistry
- blocking peptide available (sc-6227 P), 100 µg/0 5 ml: $45

CKR-2B (C-20): *cat # sc-6228*

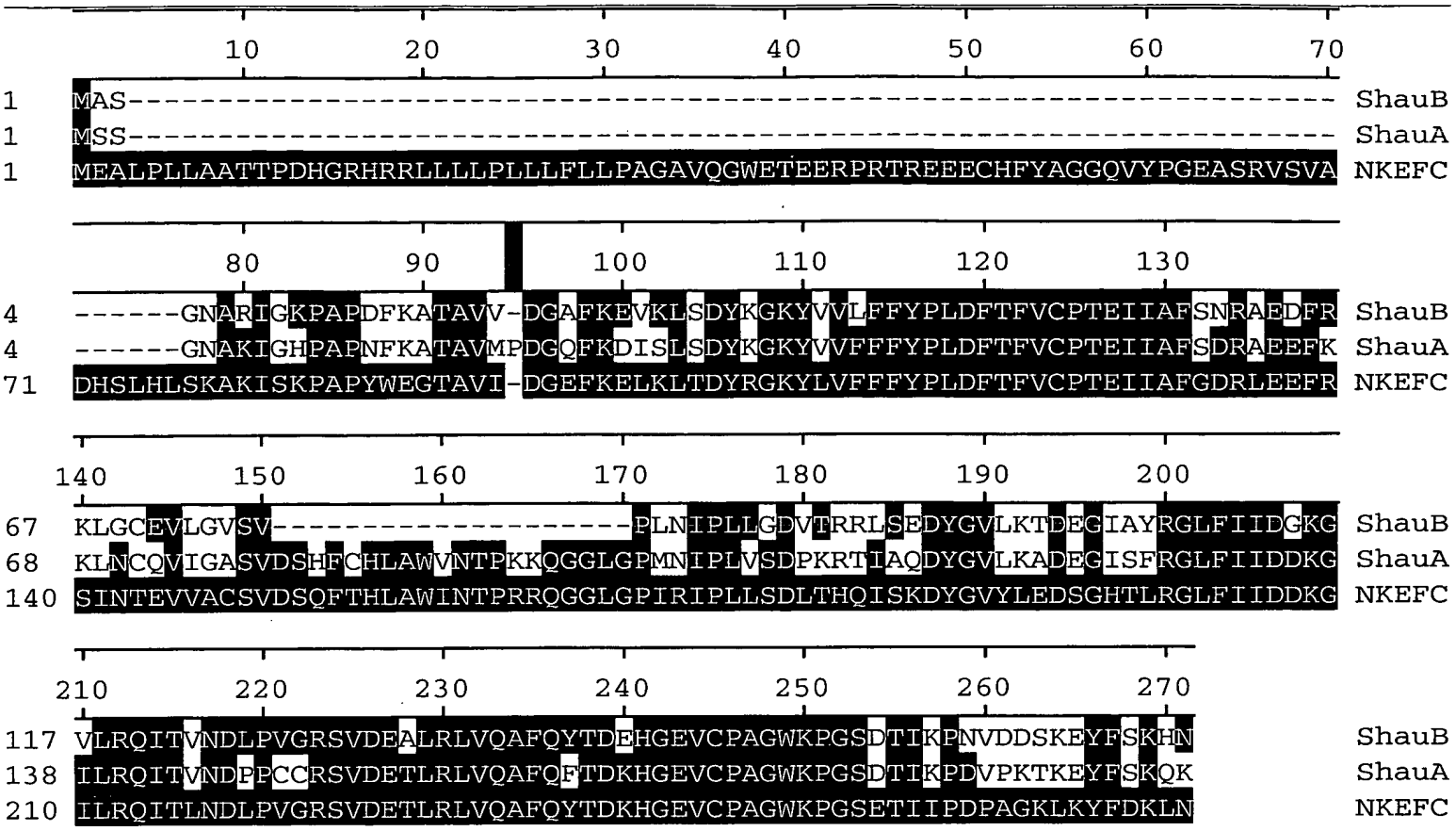
- goat polyclonal IgG, 200 µg/ml: $175
- epitope corresponding to amino acids 341-360 mapping at the carboxy terminus of the C-C chemokine receptor gene type 2B (CKR-2B) precursor of human origin
- specific for CKR-2B; non cross-reactive with other known C-C chemokine receptor gene-encoded proteins
- mouse, rat and human reactive
- Western blotting and immunohistochemistry
- blocking peptide available (sc-6228 P), 100 µg/0.5 ml: $45

CKR-3 (M-19): *cat # sc-6130*

- goat polyclonal IgG, 200 µg/ml: $175
- epitope corresponding to amino acids 341-359 mapping at the carboxy terminus of the C-C chemokine receptor gene type 3 (CKR-3) precursor of mouse origin
- specific for CKR-3; non cross-reactive with other known C-C chemokine receptor gene-encoded proteins
- mouse and rat reactive
- Western blotting and immunohistochemistry
- blocking peptide available (sc-6130 P), 100 µg/0 5 ml: $45

CKR-3 (C-20): *cat # sc-6225*

- goat polyclonal IgG, 200 µg/ml: $175
- epitope corresponding to amino acids 336-355 mapping at the carboxy terminus of the C-C chemokine receptor gene type 3 (CKR-3) precursor of human origin
- specific for CKR-3; non cross-reactive with other known C-C chemokine receptor gene-encoded proteins
- human reactive
- Western blotting and immunohistochemistry
- blocking peptide available (sc-6225 P), 100 µg/0 5 ml: $45



Decoration 'Decoration #1': Shade (with solid black) residues that match NKEFC.PRO exactly.

Decoration 'Decoration #2': Shade (with solid black) residues that match NKEFC.PRO exactly.